DATA EVALUATION RECORD

Low pH Phenolic 256
(o-Phenylphenol and o-Benzyl-p-chlorophenol)

Study Type: Acute Six Pack (81-1, -2, -3, and -6)

Work Assignment No. 2-36B (D228579)

Prepared for

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Date: 11/11/96

Disclaimer

This Data Evaluation Record may have been altered by the Registration Division subsequent to signing by Dynamac Corporation personnel.

EPA Reviewer: _____, Date _____
Review Section __, Toxicology Branch __ (7505W)
EPA Secondary Reviewer: _____, Date _____
Review Section __, Toxicology Branch __ (7505W)

DATA EVALUATION RECORD

STUDY TYPE: Acute Oral Toxicity - Rat
OPPTS 870.1100 [§81-1]

DP BARCODE: D228579 SUBMISSION CODE:
P.C. CODE: 064103 and 062201 TOX. CHEM. NO.:
EPA REG. NO.: 211-AE

TEST MATERIAL (PURITY): Low pH Phenolic RDP-4A 03-22-95 (8.085% o-phenylphenol and 6.650% o-benzyl-p-chlorophenol)

SYNONYMS: Low pH Phenolic 256

CITATION: Cerven, D. (1995) Single dose oral toxicity in rats. MB Research Laboratories, Inc., Spinnerstown, PA. Laboratory Project ID MB 95-4506A. September 7, 1995. MRID 43973406. Unpublished.

SPONSOR: Central Solutions, Inc. (address not provided)

EXECUTIVE SUMMARY: In an acute oral toxicity study (MRID 43973406), a group of five young adult Wistar albino rats/sex was given a single oral dose of Low pH Phenolic RDP-4A 03-22-95 (8.085% o-phenylphenol and 6.650% o-benzyl-p-chlorophenol) at 5,000 mg/kg (limit concentration). The test substance was administered as received. Animals were observed for clinical signs of toxicity and mortality for up to 14 days postdosing.

Oral LD_{50} Males = >5,000 mg/kg (observed)
Females = <5,000 mg/kg (observed)
Combined = ≥5,000 mg/kg (observed)

An accurate **TOXICITY CATEGORY** for Low pH Phenolic RDP-4A 03-22-95 could not be determined.

Four females died within 3 days of test substance administration; all males survived the 14-day observation period. Signs of toxicity were observed in all animals within 2 hours of administration. Effects observed during the study included lethargy, ataxia, wetness/soiling of the anogenital area, nose/mouth area stained brown, flaccid muscle tone, prostration, piloerection, chromorhinorrhea, hunched posture, dyspnea, chromodacryorrhea, diarrhea, and emaciation. Effects subsided from the single surviving female by day 3, and from all males by day 8. The body weight of the single surviving female decreased (2.5%) between 0 and 7 days. Overall (0-14 days), however, this animal exhibited an increase of 21%. No significant treatment-

related effects on body weight were observed in male animals. Gross necropsy of the decedent females revealed abnormalities of the lungs, stomach, intestines, adrenals, and liver. Necropsy of animals sacrificed after 14 days revealed stomach adhesion to the body cavity and liver in a single male.

Since an accurate LD_{50} value for female animals was not established, this study is classified **unacceptable (81-1)**. Alone, this study does not satisfy the guideline requirement for an acute oral study in the rat. For complete fulfillment of guideline requirements, additional data on the acute oral toxicity of Low pH Phenolic RDP-4A 03-22-95 for female animals must be submitted.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

I. MATERIALS AND METHODS

A. MATERIALS:

1. Test Material: Low pH Phenolic RDP-4A 03-22-95
   Description: Clear amber liquid
   Lot/Batch #: Not specified
   Composition: 8.085% o-Phenylphenol and 6.650% o-benzyl-p-chlorophenol
   Specific gravity: 1.11
   CAS #: 90-43-7 and 120-32-1, respectively

2. Vehicle: None employed.

3. Test animals: Species: Rat
   Strain: Wistar albino
   Age: Young adult (8-11 weeks)
   Weight: 228-259 g males; 200-238 g females
   Source: Ace Animals, Inc., Boyertown, PA
   Acclimation period: ≥1 Week
   Diet: Purina Rat Chow (#5012), ad libitum
   Water: Tap water, ad libitum
   Housing: Five/sex/cage

B. STUDY DESIGN and METHODS:

1. In-life dates: June 16-30, 1995

2. Animal assignment and treatment: Following a 16- to 20-hour fasting period, five young adult rats/sex were given a single oral dose of Low pH Phenolic RDP-4A 03-22-95 at 5,000 mg/kg (limit concentration) by gavage. The test substance was administered as received. The rats were observed for signs of

toxicity and/or mortality at 1, 2, and 4 hours following treatment, and at least once daily thereafter for the remainder of the 14-day study; body weights were recorded at 0 (prior to dosing), 7, and 14 days. At 14 days, the surviving animals were sacrificed, and all animals were necropsied and examined for gross pathological changes.

3. Statistics: None employed.

II. RESULTS AND DISCUSSION:

A. Mortality: Four females died within 3 days of test substance administration; all males survived the 14-day observation period.

Oral LD_{50} Males = >5,000 mg/kg (observed)
Females = <5,000 mg/kg (observed)
Combined = ≥5,000 mg/kg (observed)

B. Clinical observations: Within 2 hours of administration, lethargy, ataxia, flaccid muscle tone, and prostration were observed in all females. Additional effects observed in the two female animals surviving beyond day 1 included wetness of the anogenital area, nose/mouth area stained brown, piloerection, chromorhinorrhea, and hunched posture. Effects subsided from the single surviving female by day 3.

Effects observed in male animals included lethargy (5/5), ataxia (5/5), wetness of the anogenital area (5/5), nose/mouth area stained brown (2/5), dyspnea (1/5), chromodacryorrhea (1/5), diarrhea (1/5), soiling of the anogenital area (1/5), and emaciation (1/5). Effects subsided from 4/5 males by day 4 and from 5/5 males by day 8.

C. Body Weight: The body weight of the single surviving female decreased (2.5%) between 0 and 7 days. Overall (0-14 days), however, this animal exhibited an increase of 21%. No significant treatment-related effects on body weight were observed in male animals, with overall increases of 27-46% (mean of 36%)[1].

D. Necropsy: Gross necropsy of the four decedent females revealed abnormalities of the lungs (dark and/or with

[1]Although emaciation was observed in a single male animal between days 4 and 6, this animal exhibited increases between 0-7 and 7-14 days of 1.3 and 25%, respectively.

red areas), stomach (red and distended), intestines (red and/or pale areas and distended), adrenals (dark), and liver (misshapen). Necropsy of animals sacrificed after 14 days revealed stomach adhesion to the body cavity and liver in a single male.

E. Deficiencies: Since 4/5 female animals died at the limit concentration, an oral LD_{50} value for female animals was not established. As a result, this study does not fulfill Subdivision F guidelines and is deemed unacceptable (81-1). For complete fulfillment of guideline requirements, additional data on the acute oral toxicity of Low pH Phenolic RDP-4A 03-22-95 for female animals must be submitted.

EPA Reviewer: _____, Date _____
Review Section __, Toxicology Branch __ (7505W)
EPA Secondary Reviewer: _____, Date _____
Review Section __, Toxicology Branch __ (7505W)

DATA EVALUATION RECORD

STUDY TYPE: Acute Dermal Toxicity - Rabbit
OPPTS 870.1200 [§81-2]

DP BARCODE: D228579 SUBMISSION CODE:
P.C. CODE: 064103 and 062201 TOX. CHEM. NO.:
EPA REG. NO.: 211-AE

TEST MATERIAL (PURITY): Low pH Phenolic RDP-4A 03-22-95 (8.085% o-phenylphenol and 6.650% o-benzyl-p-chlorophenol)

SYNONYMS: Low pH Phenolic 256

CITATION: Cerven, D. (1995) Acute dermal toxicity/LD_{50} in rabbits. MB Research Laboratories, Inc., Spinnerstown, PA. Laboratory Project ID MB 95-4506B. September 7, 1995. MRID 43973404. Unpublished.

SPONSOR: Central Solutions, Inc. (address not provided)

EXECUTIVE SUMMARY: In an acute dermal toxicity study (MRID 43973404), five young adult New Zealand albino rabbits/sex were dermally exposed to Low pH Phenolic RDP-4A 03-22-95 (8.085% o-phenylphenol and 6.650% o-benzyl-p-chlorophenol) at 2,000 mg/kg (limit concentration) for 24 hours. The test substance was administered as received to approximately 10% of the total body surface. Animals were observed for clinical signs of toxicity and mortality for up to 14 days postdosing.

Dermal LD_{50} Males = >2,000 mg/kg (observed)
Females = >2,000 mg/kg (observed)

Low pH Phenolic RDP-4A 03-22-95 is classified as **TOXICITY CATEGORY III** based on the observed LD_{50} values for both sexes.

All animals survived the 14-day observation period. Diarrhea was observed in three females between days 1 and 5, and in three males between days 5 and 14. In addition, yellow nasal discharge and few feces were observed in a single female from 3-7 days, and soiling of the anogenital area was observed in two males on day 14. Well-defined erythema and edema were observed at all treatment sites 1 day following treatment; irritation progressed to severe at 9/10 sites by 7 days. At 14 days, very slight edema persisted at 4/10 sites. No treatment-related effect on body weight was observed in female animals. In contrast, the body weights of two males remained unchanged between 0 and 7 days following application, and of 1/2 continued to remain unchanged

between 7 and 14 days. Gross necropsy of animals sacrificed after 14 days revealed no treatment-related internal abnormalities.

This study is classified **acceptable (81-2)**, and satisfies the guideline requirement for an acute dermal study in the rabbit.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

I. MATERIALS AND METHODS

A. MATERIALS:

1. Test Material: Low pH Phenolic RDP-4A 03-22-95
   Description: Clear amber liquid
   Lot/Batch #: Not specified
   Composition: 8.085% o-Phenylphenol and 6.650% o-benzyl-p-chlorophenol
   Specific gravity: 1.11
   CAS #: 90-43-7 and 120-32-1, respectively

2. Vehicle: None employed

3. Test animals: Species: Rabbit
   Strain: New Zealand albino
   Age: Young adult (11-13 weeks)
   Weight: 2.5-2.7 kg males; 2.0-2.4 kg females
   Source: Ace Animals, Inc., Boyertown, PA
   Acclimation period: ≥1 Week
   Diet: Purina Rabbit Chow (#5321), unspecified amount/animal/day
   Water: Tap water, ad libitum

B. STUDY DESIGN and METHODS:

1. In life dates: June 21-July 5, 1995

2. Animal assignment and treatment: Fur from the dorsal trunk areas (approximately 10% of the total body surface area) of five animals/sex was clipped approximately 24 hours prior to dermal administration of Low pH Phenolic RDP-4A 03-22-95 at 2,000 mg/kg (limit concentration). The test substance was applied as received to the entire clipped site. Following application, the test site was covered (using gentle pressure) with a 4-ply 4 x 6-inch gauze patch, and the entire torso was wrapped with plastic secured with non-irritating tape. After 24 hours, the coverings were removed, and each application site was gently washed with distilled

water. The rabbits were observed for signs of toxicity and/or mortality at 1, 2, and 4 hours following treatment, and at least once daily thereafter for the remainder of the 14-day study. Dermal irritation was observed at 1, 7, and 14 days following application and scored separately for erythema and edema according to the Draize scheme. In addition, body weights were recorded at 0 (prior to dosing), 7, and 14 days. At 14 days, the surviving animals were sacrificed, necropsied, and examined for gross pathological changes.

3. Statistics: Not applicable to this study.

II. **RESULTS AND DISCUSSION:**

A. Mortality: All animals survived the 14-day observation period.

Dermal LD_{50} Males = >2,000 mg/kg (observed)
Females = >2,000 mg/kg (observed)

B. Clinical observations: Diarrhea was observed in three females between days 1 and 5, and in three males between days 5 and 14. In addition, yellow nasal discharge and few feces were observed in a single female from 3-7 days, and soiling of the anogenital area was observed in two males on day 14. Two animals/sex exhibited no signs of systemic toxicity during the 14-day observation period.

One day following application, well-defined erythema (score of 2) and slight edema (score of 2) were observed at all treatment sites. Irritation worsened by 7 days, and included severe erythema to moderate eschar formation at 9/10 sites, slight edema (score of 2) at 10/10 sites, and flaking skin at 3/10 sites. At 14 days, very slight edema (score of 1) persisted at 4/10 sites; edema had subsided at all sites by 14 days.

C. Body Weight: The body weights of two males remained unchanged between 0 and 7 days following application, and of 1/2 continued to remain unchanged between 7 and 14 days. Overall (0-14 days), 4/5 males exhibited increases of 9.8%, and all females gained weight during the study, with an overall average increase of 17%.

D. Necropsy: Aside from skin irritation and anogenital staining observed during the study, gross necropsy of animals sacrificed after 14 days revealed no treatment-related abnormalities.

E. Deficiencies: Subdivision F guidelines specify that the study should be conducted for 14 days, or until all animals appear normal. Although this study was terminated at 14 days, at which time anogenital staining was observed in two males and very slight edema persisted at 4/10 application sites, this deficiency does not alter the results of the study, and is considered minor.

EPA Reviewer: _____, Date _____
Review Section __, Toxicology Branch __ (7505W)
EPA Secondary Reviewer: _____, Date _____
Review Section __, Toxicology Branch __ (7505W)

DATA EVALUATION RECORD

STUDY TYPE: Acute Inhalation Toxicity - Rat
OPPTS 870.1300 [§81-3]

DP BARCODE: D228579 SUBMISSION CODE:
P.C. CODE: 064103 and 062201 TOX. CHEM. NO.:
EPA REG. NO.: 211-AE

TEST MATERIAL (PURITY): Low pH Phenolic RDP-4A 03-22-95 (8.085% o-phenylphenol and 6.650% o-benzyl-p-chlorophenol)

SYNONYMS: Low pH Phenolic 256

CITATION: Cerven, D. (1995) Inhalation toxicity in rats. MB Research Laboratories, Inc., Spinnerstown, PA. Laboratory Project ID MB 95-4506E. September 7, 1995. MRID 43973402. Unpublished.

SPONSOR: Central Solutions, Inc. (address not provided)

EXECUTIVE SUMMARY: In an acute inhalation toxicity study (MRID 43973402), a group of five young adult Wistar albino rats/sex were exposed by whole-body inhalation to Low pH Phenolic RDP-4A 03-22-95 (8.085% o-phenylphenol and 6.650% o-benzyl-p-chlorophenol) at a gravimetrically-determined concentration of 2.3 mg/L (>limit concentration) for 4 hours. Animals were observed for clinical signs of toxicity and mortality for up to 14 days postexposure.

Inhalation LC_{50} Males = >2.3 mg/L (observed)
Females = >2.3 mg/L (observed)

Low pH Phenolic RDP-4A is classified as **TOXICITY CATEGORY IV** based on the observed LC_{50} values for both sexes.

One male died 1 day following exposure. Effects observed prior to death included dyspnea, lethargy, ocular abnormalities, nose/mouth area wet and stained red, fur coated with test material, hunched posture, gasping, and labored breathing. Similar effects were observed in surviving animals. In addition, respiratory distress, an unkempt appearance, wetness of the anogenital area, piloerection, emaciation, a bloated abdomen, and alopecia around eye or on the back were observed in surviving animals during the 14-day observation period. Aside from alopecia, effects subsided from all surviving animals by day 13. A significant treatment-related effect on body weight was observed in both sexes. Three surviving males and all females

exhibited weight losses between 0 and 7 days following exposure. All surviving animals then gained weight between 7 and 14 days. Overall, all surviving males gained weight; in contrast, 2/5 surviving females exhibited overall decreases of 2.0-2.3%. Necropsy of the single decedent male revealed abnormalities of the lungs, pleural cavity, kidneys, intestines, and eyes. No significant findings were revealed upon necropsy of animals sacrificed after 14 days.

This study is classified **acceptable (81-3)**, and satisfies the guideline requirement for an acute inhalation study in the rat.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

I. MATERIALS AND METHODS

A. MATERIALS:

1. Test Material: Low pH Phenolic RDP-4A 03-22-95
   Description: Clear amber liquid
   Lot/Batch #: Not specified
   Composition: 8.085% o-Phenylphenol and 6.650% o-benzyl-p-chlorophenol
   Specific gravity: 1.11
   CAS #: 90-43-7 and 120-32-1, respectively

2. Vehicle and/or positive control: None employed

3. Test animals: Species: Rat
   Strain: Wistar albino
   Age: Young adult (9-12 weeks)
   Weight: 279-300 g males; 254-275 g females
   Source: Ace Animals, Inc., Boyertown, PA
   Acclimation period: ≥1 Week
   Diet: Purina Rat Chow (#5012), ad libitum, except during exposure
   Water: Tap water, ad libitum, except during exposure

B. STUDY DESIGN and METHODS:

1. In-life dates: June 20-July 4, 1995

2. Exposure conditions: A whole-body, dynamic-flow exposure chamber (57 L) constructed of glass and designed to ensure uniform spatial distribution of aerosol and continuous animal observation was used. Ten internal pie-shaped partitions were constructed with wire screening for animal containment during exposure.

Test atmosphere was generated using a Spraying Systems Model 1/8 JBC atomizing nozzle operated with pre-filtered compressed air. Test material was pumped from a 100-mL syringe using a Harvard Infusion Pump into the atomizing nozzle. The airflow through the chamber was maintained at 30 L/min (equivalent to 32 turnovers/hour). The time required for equilibration was not provided.

The nominal test atmosphere concentration was calculated at the end of the exposure period by dividing the total amount of test material delivered to the chamber by the total air volume passing through the chamber during the exposure time. The total solid composition of the test aerosol was 90%, as determined in preliminary experiments. As a result, the actual test atmosphere concentration was measured gravimetrically at six unspecified times during exposure; samples were collected from an unspecified site at a rate of 3 L/min for 2 minutes per sampling event. The nominal and average analytical test concentrations were 12.9 and 2.3 mg/L, respectively.

Particle size was determined at two unspecified times during the exposure period using an 8-stage Anderson Cascade Impactor at a rate of 28.3 L/min for 2 minutes. The calculated average mass median aerodynamic diameter (MMAD) and geometric standard deviation (GSD) were 0.85 and 2.30 µm, respectively. One hundred percent of the particles were ≤5.8 µm.

During the exposure period, the temperature ranged from 24.0 to 26.4 °C (75.2 to 79.5 °F) and the humidity of the atmosphere entering the chamber ranged from 88 to 90%. Although not monitored, the turnover rate ensured an oxygen concentration of ≥19%.

3. Animal assignment and treatment: Five rats/sex were exposed to Low pH Phenolic RDP-4A 03-22-95 at 2.3 mg/L (>limit concentration) by whole-body inhalation for 4 hours. The animals were observed for signs of toxicity and/or mortality hourly during exposure, 1 hour following exposure, and at least once daily thereafter for the remainder of the 14-day study; body weights were recorded at 0 (prior to exposure), 7, and 14 days. After 14 days, all animals were sacrificed, and all animals (upon death) were necropsied and examined for gross pathological changes.

4. Statistics: Not applicable to this study.

II. RESULTS AND DISCUSSION:

A. Mortality: One male died 1 day following exposure; all remaining animals survived the 4-hour exposure and 14-day observation periods.

Inhalation LC_{50} Males = >2.3 mg/L (observed)
Females = >2.3 mg/L (observed)

B. Clinical observations: Clinical effects observed at 210 minutes into the exposure period included eyes closed (10/10), nose/mouth area wet and stained red (10/10), fur coated with test material (10/10), eyes crusting/lacrimation (10/10), hunched posture (10/10), gasping (7/10), labored breathing (3/10), and respiratory distress (3/10). Additional effects observed 1 hour following exposure included lethargy (10/10), dyspnea (10/10), and red and swollen eyes (6/10). Additional effects observed in surviving animals during the 14-day observation period included an unkempt appearance (8/9), wetness of the anogenital area (8/9), piloerection (4/9), emaciation (2/9), a bloated abdomen (1/9), and alopecia around eye (1/9) or on the back (1/9). Aside from alopecia, effects subsided from all surviving animals by day 13; alopecia persisted from days 9 through 14.

C. Body Weight: A significant treatment-related effect on body weight was observed in both sexes. Three surviving males and all females exhibited weight losses between 0 and 7 days following exposure. All surviving animals then gained weight between 7 and 14 days. Overall (0-14 days), all surviving males gained weight, with an average increase of 16%. In contrast, 2/5 surviving females exhibited overall decreases of 2.0-2.3%. The remaining three females gained an overall 3.9-7.3%.

D. Necropsy: Necropsy of the single decedent male revealed dark lungs with red areas, excess fluid in the pleural cavity, hydronephrotic kidneys, large right kidney, distended intestines with red areas, and opaque eyes. Necropsy of animals sacrificed after 14 days revealed alopecia in 3/9 animals.

E. Deficiencies: The aerodynamic particle size should have been determined hourly during the exposure. Since the size was determined twice, and since the calculated MMAD and GSD values were comparable and within the ideal limits of 1-4 μm, this deficiency is considered minor.

The site of sample collection was not specified for either particle size or concentration measurements. However, based on the degree of variability of the animals' orientation in the exposure chamber, it is most likely that the samples were collected from an appropriate position, and this deficiency is considered minor.

Both temperature and humidity conditions exceeded limits outlined in Subdivision F guidelines. The impact of these deviations, however, are considered minor and should have had no effect on the results of this study.

EPA Reviewer: _____, Date _____
Review Section __, Toxicology Branch __ (7505W)
EPA Secondary Reviewer: _____, Date _____
Review Section __, Toxicology Branch __ (7505W)

DATA EVALUATION RECORD

STUDY TYPE: Dermal Sensitization - Guinea pig
OPPTS 870.2600 [§81-6]

DP BARCODE: D228579 SUBMISSION CODE:
P.C. CODE: 064103 and 062201 TOX. CHEM. NO.:
EPA REG. NO.: 211-AE

TEST MATERIAL (PURITY): Low pH Phenolic RDP-4A 03-22-95 (8.085% o-phenylphenol and 6.650% o-benzyl-p-chlorophenol)

SYNONYMS: Low pH Phenolic 256

CITATION: Newcomb, T. (1995) Delayed contact dermal sensitization test - Buehler. MB Research Laboratories, Inc., Spinnerstown, PA. Laboratory Project ID MB 95-4506F. September 7, 1995. MRID 43973401. Unpublished.

SPONSOR: Central Solutions, Inc. (address not provided)

EXECUTIVE SUMMARY: In a dermal sensitization study (MRID 43973401) conducted with Low pH Phenolic RDP-4A 03-22-95 (8.085% o-phenylphenol and 6.650% o-benzyl-p-chlorophenol), 15 male Hartley albino guinea pigs (ten test and five control) were tested using methods based on those derived by Buehler. Data were provided from a positive control study (MB Research Laboratories, May 1-June 1, 1995) conducted in the same manner using dinitrochlorobenzene.

Twenty-four hours following the single challenge treatment to previously-inducted animals, very faint erythema was observed at 3/10 sites; irritation subsided by 48 hours. No dermal irritation was observed upon challenge to naive control animals. Acceptable positive control data were provided to validate the test methodology. Based on the results of this study, **Low pH Phenolic RDP-4A 03-22-95 appears to be a very slight dermal sensitizer**. This is in disagreement with the study author, who reported that the test material is not a sensitizer.

This study is classified **acceptable (81-6)**, and satisfies the guideline requirement for a dermal sensitization study in the guinea pig.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

I. MATERIALS AND METHODS

A. MATERIALS:

1. Test Material: Low pH Phenolic RDP-4A 03-22-95
   Description: Clear amber liquid
   Lot/Batch #: Not specified
   Composition: 8.085% o-Phenylphenol and 6.650% o-benzyl-p-chlorophenol
   Specific gravity: 1.11
   CAS #: 90-43-7 and 120-32-1, respectively

2. Vehicle and positive control: Distilled water was used as a test substance vehicle for the second and third induction treatments and challenge treatment.

   Positive control data from a previously-conducted study (May 1-June 1, 1995) were provided using 0.2% (w:v) dinitrochlorobenzene (DNCB; purity not specified) in 80% aqueous ethanol (induction phase) or 0.1% (w:v) DNCB in acetone (challenge phase).

3. Test animals: Species: Guinea pig
   Strain: Hartley albino
   Age: Young adult (approximately 4 weeks)
   Weight: 405-542 g (preliminary study, all males) and 336-400 g (definitive study, all males)
   Source: Ace Animals, Inc., Boyertown, PA
   Acclimation period: ≥5 Days
   Diet: Purina Guinea Pig Chow (#5025), ad libitum
   Water: Tap water, ad libitum

B. STUDY DESIGN and METHODS:

1. In-life dates: June 21-July 22, 1995

2. Animal assignment and treatment: The study was conducted using methods based on those derived by Buehler (reference not cited). To determine the highest non-irritating dose, preliminary experiments were conducted with eight male animals and dose levels of 0.1, 0.5, 1.0, 2.5, 5, 10, 25, or 50% Low pH Phenolic RDP-4A 03-22-95 in distilled water. Based on the results of these experiments, the highest non-irritating dose was 2.5% (reviewer's judgment). No explanation was provided by the study author for administration of the test material as received (100%) for the first induction treatment of the definitive study. Since this treatment elicited moderate to severe erythema at all test sites, the concentration was changed to 5% for the second and third induction treatments. A 1% concentration was

used for the challenge treatment in the definitive study.

For the induction phase, fur from the dorsal trunk areas of ten male animals was clipped 24 hours prior to dermal administration of 0.4 mL of undiluted Low pH Phenolic RDP-4A 03-22-95 using a 25-mm Hilltop Chamber; application was to a single site/animal near the left shoulder. Each chamber was covered with occlusive dental dam and secured with adhesive tape. Following a 6-hour exposure period, the coverings were removed, and the test sites were gently washed with distilled water and soft toweling. Application of the test substance was repeated once weekly for 2 consecutive weeks (total of three applications). Due to the severity of irritation observed following the first induction application, the second and third treatments were conducted with a 5% aqueous dilution and were made to the right shoulder region. The positive control induction phase was conducted with 0.4 mL of 0.2% DNCB solution and otherwise in the same manner as described; for the third DNCB induction treatment, the dosing site was moved to the right shoulder area to avoid application to necrotic skin.

For the challenge phase, a single treatment was applied using 0.4 mL of a 1% aqueous dilution and otherwise in the same manner as described to a previously untreated left mid-section site of each animal 14 days following the final induction treatment. The positive control challenge phase was conducted with 0.4 mL of 0.1% DNCB solution and otherwise in the same manner as described. To serve as naive controls, an additional five male animals per material were included for the challenge treatments.

The guinea pigs were observed for dermal irritation 24 and 48 hours following each induction and challenge exposure and 72 hours following the challenge treatments only. Skin reactions were scored according to the following scale:

0 - No erythema
0.5 - Very faint erythema, usually non-confluent
1 - Faint erythema, usually confluent
2 - Moderate erythema
3 - Severe erythema, with or without edema

Body weights of each animal were recorded pretest, 1 day following the last induction treatment, and 1

day following the challenge treatment.

II. RESULTS AND DISCUSSION:

A. Induction reactions and duration: Twenty-four hours following the first induction treatment (at 100%), moderate to strong erythema (score of 2-3) and very slight to slight edema were observed at 10/10 application sites; brown areas were also observed at 3/10 sites. Twenty-four hours following the second or third induction treatments (at 5%), very faint to moderate erythema (score of 0.5-2) were observed at 10/10 sites. In addition, very slight to slight edema developed at 9/10 sites 48 hours following the final induction treatment.

B. Challenge reactions and duration: Twenty-four hours following the single challenge treatment to previously-inducted animals, very faint erythema (score of 0.5) was observed at 3/10 sites; irritation subsided by 48 hours. No dermal irritation was observed upon challenge to naive control animals. Based on the results of this study, Low pH Phenolic RDP-4A 03-22-95 appears to be a very slight dermal sensitizer. This is in disagreement with the study author, who reported that the test material is not a sensitizer.

All animals appeared normal during the study, and no significant treatment-related effects on body weight were observed between animals from the treated and naive control groups, with overall increases of 50 and 59%, respectively.

C. Positive control: Since the application site was adjusted for the third induction treatment, irritation was most severe 48 hours following the second application, and included strong erythema to moderate eschar formation at 10/10 sites, moderate edema at 10/10 sites, and black areas at 8/10 sites.

Twenty-four through 72 hours following a single challenge treatment to previously-induced animals, faint to moderate erythema (scores of 0.5-2) was observed at 10/10 sites and very slight to moderate edema was observed at 7/10 sites. In comparison, very faint to faint erythema (scores of 0.5-1) was observed at 5/5 sites 24 and 48 hours after challenge to naive control animals, and at 3/5 sites after 72 hours. No edema was observed at control sites. These data confirm the adequacy of the test species and methods employed.

D. Since the test material was applied at a much higher concentration than slightly irritating for the first induction treatment, and since a slight sensitizing potential may exist, additional data on the dermal sensitization of Low pH Phenolic RDP-4A 03-22-95 may be required.

E. Deficiencies: Preliminary experiments indicated that the highest non-irritating concentration of Low pH Phenolic RDP-4A in distilled water was 2.5%, and that the slightly irritating concentration was 5%. However, the test material was used as received (100%) for the first induction treatment of the definitive study, and no explanation was provided by the study author. The effects of this deviation on the results of the study are unknown.